

104 (New) A kit for treating cancer, comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a compound comprising:

- 5 a) a chelator;
- b) a targeting moiety;
- c) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is an indazole nonpeptide that
10 binds to a receptor that is upregulated during angiogenesis.

Remarks

This is in response to the Restriction Requirement under 35 U.S.C. § 121, that was mailed
15 April 4, 2001.

After the carrying out the amendments, claims 37-50, 58-104 will be pending.

The marked-up version of amended claims is found in Appendix I, attached to this Response, and titled "Marked-Up
20 Version of Rewritten Claims". The amendments are shown by text stricken through to indicate deletions and underlined text to indicate insertions.

Claim 58 is amended to particularly point out and distinctly claim that which Applicants regard as their
25 invention. In particular, claim 58 is amended to include the material of claim 2, which has been canceled. Support for the amendment is found throughout the application, for example on page 84, lines 15-21 and page 14, line 1 to page 31, line 4.
30 Accordingly, no new matter is added.

Claim 59 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 59 is amended to include the material of claim 2, which has been canceled.
35 Support for the amendment is found throughout the

application, for example on page 84, lines 23-33.

Accordingly, no new matter is added.

5 Claim 65 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 65 is amended to include the material of claim 11, which has been canceled. Support for the amendment is found throughout the application, for example on page 86, lines 28-35, and on page 12, lines 27-32.

10 Accordingly, no new matter is added.

 Claim 66 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 66 is amended to correct antecedent basis in the claim, in light of the
15 amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

 Claim 67 is amended to particularly point out and distinctly claim that which Applicants regard as their
20 invention. In particular, claim 67 is amended to correct antecedent basis in the claim, in light of the amendment to claim 65. Support for the amendment is found throughout the application. Accordingly, no new matter is added.

25 Claim 68 is amended to particularly point out and distinctly claim that which Applicants regard as their invention. In particular, claim 68 is amended to include the material of claim 19, which has been
30 canceled. Support for the amendment is found throughout the application, for example on page 13, lines 25-31, page 87 lines 36 to page 88 line 5 and on page 12, lines 27-32. Accordingly, no new matter is added.

New claim 76 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example in original claim 3, and 59. Accordingly, no new
5 matter is added.

New claim 77 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 37, line 24, to page
10 43, line 10. Accordingly, no new matter is added.

New claim 78 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 43, line 11 to page
15 44, line 15. Accordingly, no new matter is added.

New claim 79 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 84, lines 15-21, and page 45, line 1, to page
20 52, line 35. Accordingly, no new matter is added.

New claim 80 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 6-8. Accordingly, no new matter is
25 added.

New claim 81 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for on page 53, lines 10-11. Accordingly, no new matter is added.

New claim 82 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 53, lines 13-14. Accordingly, no new matter
30 is added.

New claim 83 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-15.

5 Accordingly, no new matter is added.

New claim 84 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35 and page 58, lines 1-2.

10 Accordingly, no new matter is added.

New claim 85 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page
15 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 86 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example
20 on page 86, lines 28-35, page 57, lines 8-16, and page 31, line 5, to page 37, line 23. Accordingly, no new matter is added.

New claim 87 is added to claim that which Applicants regard as their invention. Support for this
25 claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 88 is added to claim that which Applicants regard as their invention. Support for this
30 claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 89 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no new matter is added.

New claim 90 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, and page 57, lines 8-16, and page 58, lines 3-8. Accordingly, no new matter is added.

New claim 91 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 58, lines 10-14. Accordingly, no new matter is added.

New claim 92 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

New claim 93 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 86, lines 28-35, to page 58, line 18, to page 59, line 5. Accordingly, no new matter is added.

New claim 94 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, page 53, lines 16-24, and page 58, lines 1-2. Accordingly, no new matter is added.

New claim 95 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and
5 page 13, line 33, to page 31, line 4. Accordingly, no new matter is added.

New claim 96 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87,
10 line 36, to page 88, line 5, page 57, lines 8-16 and page 31, line 5, to page 37, line 22. Accordingly, no new matter is added.

New claim 97 is added to claim that which Applicants regard as their invention. Support for this claim is
15 found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 37, line 24, to page 43, line 10. Accordingly, no new matter is added.

New claim 98 is added to claim that which Applicants regard as their invention. Support for this claim is
20 found throughout the application, for example on page 87, line 36, to page 88, line 5, page 57, lines 8-16, and page 43, line 12, to page 44, line 15. Accordingly, no new matter is added.

New claim 99 is added to claim that which Applicants regard as their invention. Support for this claim is
25 found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 45, line 1, to page 52, line 35. Accordingly, no
30 new matter is added.

New claim 100 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16,

and page 58, lines 4-8. Accordingly, no new matter is added.

5 New claim 101 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 10-14. Accordingly, no new matter is added.

10 New claim 102 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, lines 15-16. Accordingly, no new matter is added.

15 New claim 103 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 87 line 36, to page 88, line 5, page 57, lines 8-16, and page 58, line 18, to page 59, line 5. Accordingly,
20 no new matter is added.

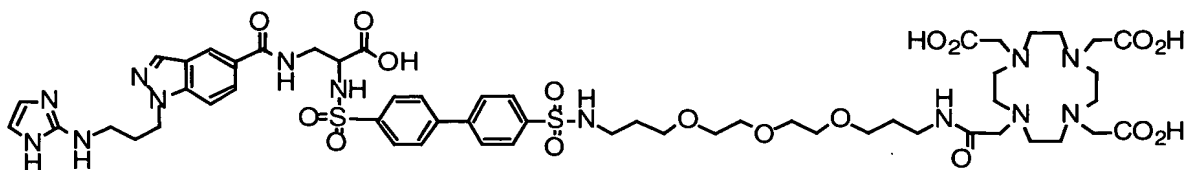
New claim 104 is added to claim that which Applicants regard as their invention. Support for this claim is found throughout the application, for example on page 93, lines 26-30, page 13, lines 25-31 and page 113,
25 lines 10-18. Accordingly, no new matter is added.

Response to Restriction Requirement

In response to the outstanding restriction requirement, Applicants provisionally elect Group V with traverse. Applicants respectfully request
30 reconsideration and modification of the restriction to include the new claims 83 to 93 which are encompassed by elected Group V.

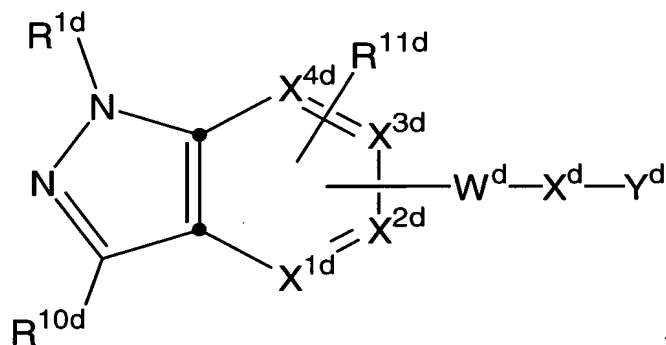
Also, as requested by the Examiner, Applicants elect Example 4, on page 142, as the species named:
35 3-((1-(3-(Imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-2-(((4-(4-(((3-(2-(2-(3-(2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclododecyl)-

acetyl amino) propoxy) ethoxy) ethoxy) propyl) amino) sulfonyl) -
phenyl) phenyl) sulfonyl) amino) propanoic acid;
having the formula:



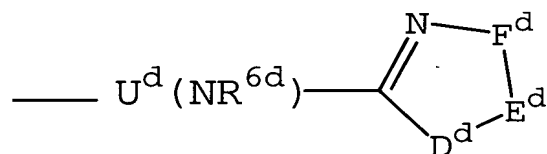
5

- Targeting Moiety: The targeting moiety is an indazole of formula:



wherein:

10 \mathbb{R}^{1d} is



wherein:

D^d is NR^{2d} and R^{2d} is H ;

$E^d - F^d$ is $CR^{4d} = CR^{5d}$ and R^{4d} and R^{5d} are H ;

15 U^d is $(CH_2)_{n^d}$ and n^d is 3;

R^{6d} is H ;

 R^{10d} is H ;

$X^{1d}, X^{2d}, X^{3d}, X^{4d}$ are C ;

R^{11d} is H;

W^d is $C(=O)N(R^{13d}) - (C(R^{12d})_2)q^d$;

R^{13d} is H;

q^d is 0;

5 X^d is $CR^{12d}R^{14d}-CR^{12d}R^{15d}-$;

R^{12d} is H;

R^{14d} is H;

R^{15d} is R^{16d} ;

R^{16d} is $N(R^{20d})SO_2R^{17d}$;

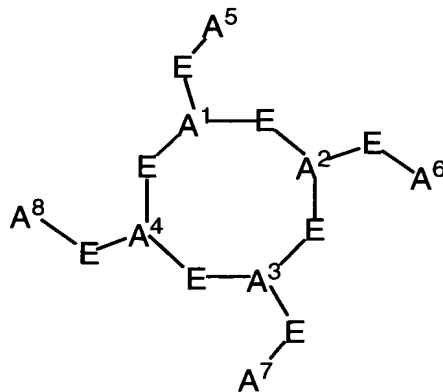
10 R^{20d} is H;

R^{17d} is a bond to Ln;

Y^d is COR^{19d} and R^{19d} is OH; and

d is 1.

- Method of Treatment: Applicants select a method of
15 treating cancer.
- Chelator: The chelator is C_h given by the formula:



wherein:

- A^1 , A^2 , A^3 , and A^4 are $NR^{13}R^{14}$ wherein R^{13} and R^{14} are
20 each an electron;

E (between A¹ and A², A² and A³, A³ and A⁴, and A⁴ and A¹) is CH₂CH₂;

A⁵, A⁶, and A⁷ are OH;

A⁸ is NR¹³R¹⁴ wherein R¹³ is H and R¹⁴ is a bond to L_n;

5 and

E (between A¹ and A⁵, A² and A⁶, A³ and A⁷, and A⁴ and A⁸) is CH₂C(=O).

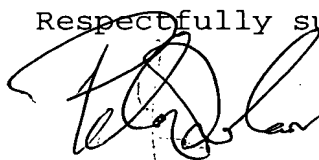
Applicants point out to the Examiner that this same compound was elected as the species in U.S. Patent application no. 09/281,207, now U.S. Patent No. 6,322,770.

Summary

Applicants submit that this application is in condition for allowance, a favorable action passing this case to issue is therefore respectfully requested. If a telephone interview would be of assistance in advancing prosecution of this application, Applicants' agent invites the Examiner to contact him at the number provided below.

20

Respectfully submitted,



25

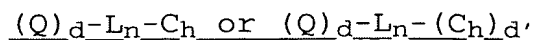
Dated: February 7, 2002

Peter L. Dolan, Ph.D.
Agent for Applicants
Registration No. 46,307
Telephone: (302) 695-7776

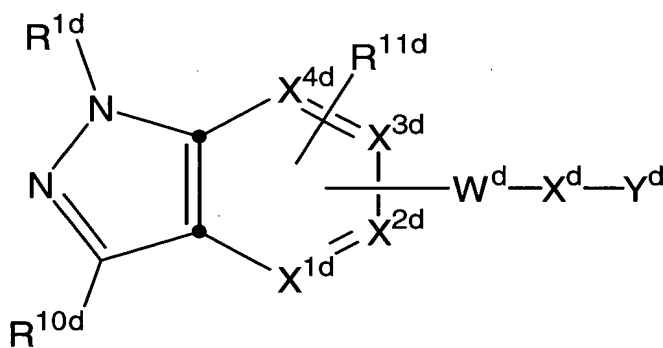
Appendix I.

Marked-Up Version of Rewritten Claims

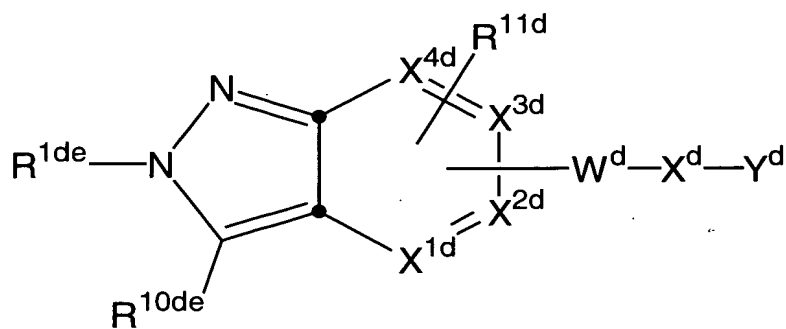
58. (Amended) A kit for treating cancer, ~~comprising a~~
 5 ~~compound of~~ according to Claim 104 ~~Claim 1~~, wherein the
compound is of the formula:



- 10 wherein, Q is independently a compound of Formula (Ia) or
(Ib):



- 15 (Ia)



(Ib)

- 20 including stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, or pharmaceutically
acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d- X^d- Y^d, or C-L_n;

X^{2d} is N, CH, or C- W^d- X^d- Y^d;

X^{3d} is N, CR^{11d}, or C- W^d- X^d- Y^d;

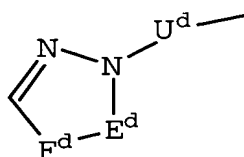
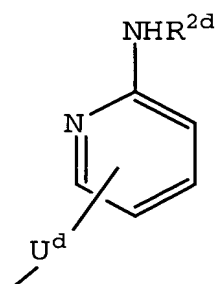
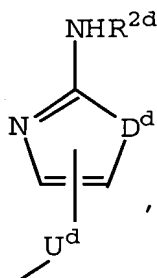
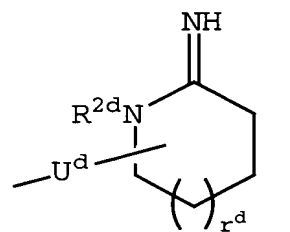
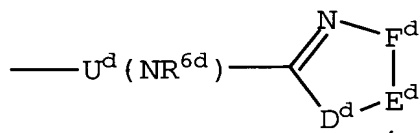
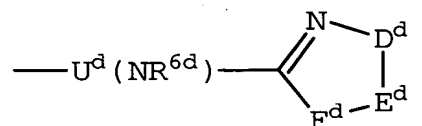
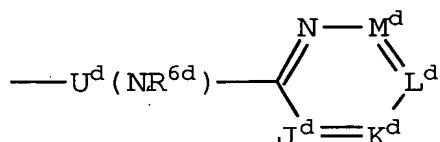
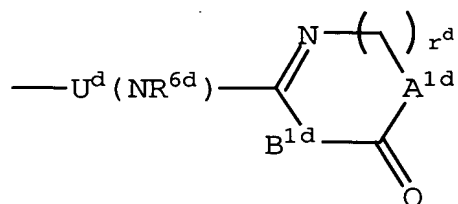
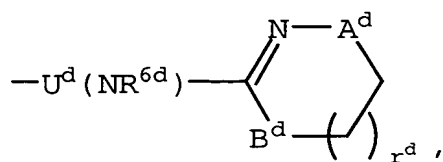
5 X^{4d} is N or CR^{11d};

provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d- X^d- Y^d, and when R^{10d} is R^{1de} then X^{3d} is C- W^d- X^d- Y^d;

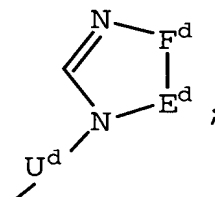
10 R^{1d} is selected from: R^{1de}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

15

R¹_{de} is selected from:



or



A^d and B^d are independently $-CH_2-$, $-O-$, $-N(R^{2d})-$, or $-C(=O)-$

A^{1d} and B^{1d} are independently -CH₂- or -N(R^{3d})-;

D^d is -N(R^{2d})-, -O-, -S-, -C(=O)- or -SO₂-;

5

E^d-F^d is -C(R^{4d})=C(R^{5d})-, -N=C(R^{4d})-, -C(R^{4d})=N-, or
-C(R^{4d})₂C(R^{5d})₂-;

J^d, K^d, L^d and M^d are independently selected from

10 -C(R^{4d})-, -C(R^{5d})- and -N-, provided that at least one of
J^d, K^d, L^d and M^d is not -N-;

R^{2d} is selected from: H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl,

15

(C₁-C₆ alkoxy)carbonyl; (C₁-C₆ alkyl)aminocarbonyl, C₃-C₆

alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl,

heteroaryl(C₁-C₆ alkyl)carbonyl, heteroarylcabonyl,

aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl-, arylcarbonyl,

C₁-C₆ alkylsulfonyl, arylsulfonyl, aryl(C₁-C₆

alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆

20

alkyl)sulfonyl, aryloxy carbonyl, and aryl(C₁-C₆

alkoxy)carbonyl, wherein said aryl groups are substituted

with 0-2 substituents selected from the group: C₁-C₄

alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro;

25

R^{3d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁

cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and

heteroaryl(C₁-C₆ alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C₁-C₄ alkoxy,

30

NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C₁-C₆ alkyl, C₃-C₆ alkenyl,

C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆

alkyl)-, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl,
and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d}
 5 can be taken together with the carbon atoms to which they
are attached to form a 5-7 membered carbocyclic or 5-7
membered heterocyclic aromatic or non-aromatic ring
system, said carbocyclic or heterocyclic ring being
optionally substituted with 0-2 groups selected from: C₁-
 10 C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, amino, CF₃, and NO₂;

U^d is selected from:

-(CH₂)_{n^d}-,
-(CH₂)_{n^d}(CR^{7d}=CR^{8d})(CH₂)_{m^d}-,
 15 -(CH₂)_{n^d}(C≡C)(CH₂)_{m^d}-,
-(CH₂)_{t^d}Q(CH₂)_{m^d}-,
-(CH₂)_{n^d}O(CH₂)_{m^d}-,
-(CH₂)_{n^d}N(R^{6d})(CH₂)_{m^d}-,
-(CH₂)_{n^d}C(=O)(CH₂)_{m^d}-,
 20 -(CH₂)_{n^d}(C=O)N(R^{6d})(CH₂)_{m^d}-
-(CH₂)_{n^d}N(R^{6d})(C=O)(CH₂)_{m^d}-, and
-(CH₂)_{n^d}S(O)_{p^d}(CH₂)_{m^d};

wherein one or more of the methylene groups in U^d is
optionally substituted with R^{7d};

25 Q^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-
phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-
pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

30 R^{6d} is selected from: H, C₁-C₄ alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and heteroaryl(C₀-C₆ alkyl)-;

5

R^{10d} is selected from: H, R^{1de}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, N(R^{6d})₂, halogen, NO₂, CN, CF₃, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, -SO₂R^{17d}, -SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

10

15

R^{10de} is selected from: H, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, N(R^{6d})₂, halogen, NO₂, CN, CF₃, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, -SO₂R^{17d}, -SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d};

20

25

R^{11d} is selected from H, halogen, CF₃, CN, NO₂, hydroxy, NR^{2d}R^{3d}, C₁-C₄ alkyl substituted with 0-1 R^{21d}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d}, aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{21d},

30

(C₁-C₄ alkoxy)carbonyl substituted with 0-1 R^{21d}, (C₁-C₄ alkyl)carbonyl substituted with 0-1 R^{21d}, C₁-C₄ alkylsulfonyl substituted with 0-1 R^{21d}, and C₁-C₄ alkylaminosulfonyl substituted with 0-1 R^{21d};

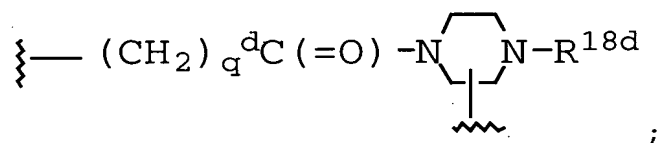
5

W^d is selected from:

-(C(R^{12d})₂)_q^dC(=O)N(R^{13d})-, and

-C(=O)-N(R^{13d})-(C(R^{12d})₂)_q^d-;

10 X^d is -C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-; or
alternatively, W^d and X^d can be taken together to be



15 R^{12d} is selected from H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, and aryl(C₁-C₆ alkyl)-;

R^{13d} is selected from H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl,
 20 and aryl(C₁-C₆ alkyl)-;

R^{14d} is selected from:

H, C₁-C₆ alkylthio(C₁-C₆ alkyl)-, aryl(C₁-C₁₀ alkylthioalkyl)-, aryl(C₁-C₁₀ alkoxyalkyl)-, C₁-C₁₀ alkyl,
 25 C₁-C₁₀ alkoxyalkyl, C₁-C₆ hydroxyalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, and CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or

heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d} ;

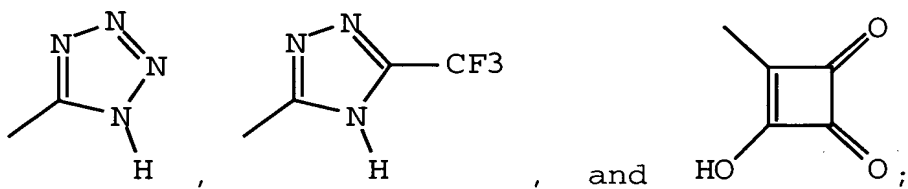
R^{15d} is selected from:

- 5 H, R^{16d} , C_1 - C_{10} alkyl, C_1 - C_{10} alkoxyalkyl,
 C_1 - C_{10} alkylaminoalkyl, C_1 - C_{10} dialkylaminoalkyl, (C_1 - C_{10}
alkyl)carbonyl, aryl(C_1 - C_6 alkyl)carbonyl, C_1 - C_{10} alkenyl,
 C_1 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, C_3 - C_{10} cycloalkylalkyl,
aryl(C_1 - C_6 alkyl)-, heteroaryl(C_1 - C_6 alkyl)-, aryl,
10 heteroaryl, CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, SO_2R^{17d} , and
 $SO_2NR^{17d}R^{20d}$, provided that any of the above alkyl,
cycloalkyl, aryl or heteroaryl groups may be
unsubstituted or substituted independently with 0-2 R^{11d} ;

- 15 Y^d is selected from:

- COR^{19d} , - SO_3H , - PO_3H , tetrazolyl, - $CONHNHSO_2CF_3$, -
 $CONHSO_2R^{17d}$, - $CONHSO_2NHR^{17d}$, - $NHCOCF_3$, - $NHCONHSO_2R^{17d}$, -
 $NHSO_2R^{17d}$, - OPO_3H_2 , - OSO_3H , - PO_3H_2 , - SO_3H , - SO_2NHCOR^{17d} , -
 $SO_2NHCO_2R^{17d}$,

20 _____



R^{16d} is selected from:

- 25 - $N(R^{20d})-C(=O)-O-R^{17d}$,
- $N(R^{20d})-C(=O)-R^{17d}$,
- $N(R^{20d})-C(=O)-NH-R^{17d}$,
- $N(R^{20d})SO_2-R^{17d}$, and
- $N(R^{20d})SO_2-NR^{20d}R^{17d}$;

R^{17d} is selected from:

C₁-C₁₀ alkyl optionally substituted with a bond to L_n, C₃-
C₁₁ cycloalkyl optionally substituted with a bond to L_n,
aryl(C₁-C₆ alkyl)- optionally substituted with a bond to
5 L_n, (C₁-C₆ alkyl)aryl optionally substituted with a bond
to L_n, heteroaryl(C₁-C₆ alkyl)- optionally substituted
with a bond to L_n, (C₁-C₆ alkyl)heteroaryl optionally
substituted with a bond to L_n, biaryl(C₁-C₆ alkyl)-
optionally substituted with a bond to L_n, heteroaryl
10 optionally substituted with a bond to L_n, aryl optionally
substituted with a bond to L_n, biaryl optionally
substituted with a bond to L_n, and a bond to L_n, wherein
said aryl, biaryl or heteroaryl groups are also
optionally substituted with 0-3 substituents selected
15 from the group consisting of: C₁-C₄ alkyl, C₁-C₄ alkoxy,
aryl, heteroaryl, halo, cyano, amino, CF₃, and NO₂;

R^{18d} is selected from:

-H,
20 -C(=O)-O-R^{17d},
-C(=O)-R^{17d},
-C(=O)-NH-R^{17d},
-SO₂-R^{17d}, and
-SO₂-NR^{20d}R^{17d};

25

R^{19d} is selected from: hydroxy, C₁-C₁₀ alkyloxy,

C₃-C₁₁ cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀
alkylcarbonyloxyalkyloxy, C₃-C₁₀
alkoxycarbonyloxyalkyloxy, C₂-C₁₀ alkoxycarbonylalkyloxy,
30 C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy,
C₅-C₁₀ cycloalkoxycarbonyloxyalkyloxy,
C₅-C₁₀ cycloalkoxycarbonylalkyloxy,

C₇-C₁₁ aryloxy carbonylalkyloxy,
C₈-C₁₂ aryloxy carbonyloxyalkyloxy,
C₈-C₁₂ aryl carbonyloxyalkyloxy,
C₅-C₁₀ alkoxyalkyl carbonyloxyalkyloxy, C₅-C₁₀ (5-alkyl-
 5 1,3-dioxa-cyclopenten-2-one-yl)methyloxy, C₁₀-C₁₄ (5-aryl-
1,3-dioxa-cyclopenten-2-one-yl)methyloxy, and
(R^{11d}) (R^{12d})N-(C₁-C₁₀ alkoxy)-;

10 R^{20d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁
cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and
heteroaryl(C₁-C₆ alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}₂;

15 m^d is 0-4;
n^d is 0-4;
t^d is 0-4;
p^d is 0-2;
q^d is 0-2; and
r^d is 0-2;

20

with the following provisos:

(1) t^d, n^d, m^d and q^d are chosen such that the number of atoms

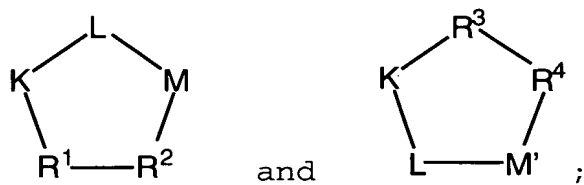
connecting R^{1d} and Y^d is in the range of 10-14; and

(2) n^d and m^d are chosen such that the value of n^d plus m^d is

25 greater than one unless U^d is

-(CH₂)_t^d Q^d (CH₂)_m^d -;

or Q is a peptide selected from the group:



R¹ is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L_n;

5

R² is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n;

10

R³ is D-valine;

R⁴ is D-tyrosine substituted on the hydroxy group with a bond to L_n;

15

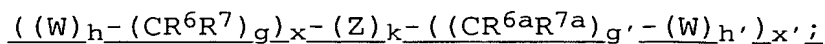
provided that one of R¹ and R² in each Q is substituted with a bond to L_n, and further provided that when R² is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

20 provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25 d' is 1-100;

L_n is a linking group having the formula:



W is independently selected at each occurrence from the group:

5 O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)N R⁸, C(=O),
C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH,
(OCH₂CH₂)_s, (CH₂CH₂O)_s', (OCH₂CH₂CH₂)_s", (CH₂CH₂CH₂O)_t, and
(aa)_t';

aa is independently at each occurrence an amino acid;

10 Z is selected from the group: aryl substituted with 0-3 R¹⁰,
C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10
membered heterocyclic ring system containing 1-4
heteroatoms independently selected from N, S, and O and
substituted with 0-3 R¹⁰;

15 R⁶, R^{6a}, R⁷, R^{7a}, and R⁸ are independently selected at each
occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C_{1-C₅}
alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3
R¹⁰, benzyl substituted with 0-3 R¹⁰, and C_{1-C₅} alkoxy
substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹,
 20 NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_h;

R¹⁰ is independently selected at each occurrence from the
group: a bond to C_h, COOR¹¹, C(=O)NHR¹¹, NHC(=O)R¹¹, OH,
NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with
 25 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy
substituted with 0-1 R¹², and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O and substituted
with 0-3 R¹¹;

30 R¹¹ is independently selected at each occurrence from the
group: H, alkyl substituted with 0-1 R¹², aryl

substituted with 0-1 R^{12} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{12} , C_{3-10} cycloalkyl substituted with 0-1 R^{12} , polyalkylene glycol substituted with 0-1 R^{12} , carbohydrate substituted with 0-1 R^{12} , cyclodextrin substituted with 0-1 R^{12} , amino acid substituted with 0-1 R^{12} , polycarboxyalkyl substituted with 0-1 R^{12} , polyazaalkyl substituted with 0-1 R^{12} , and peptide substituted with 0-1 R^{12} , wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h ;

R^{12} is a bond to C_h ;

15

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

20

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25

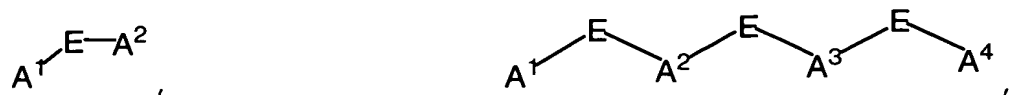
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

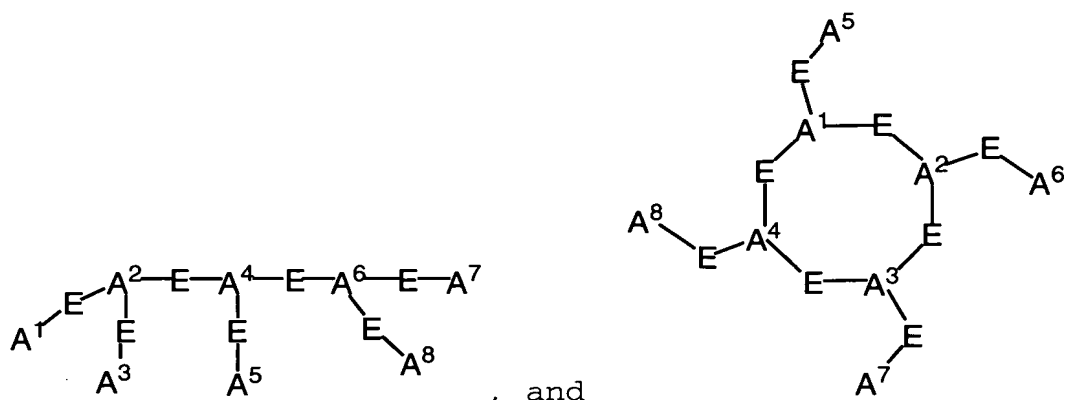
x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

30

C_h is a metal bonding unit having a formula selected from the group:





A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , and A^8 are independently selected at each occurrence from the group: NR^{13} , $NR^{13}R^{14}$, S, SH, S(Pg), O, OH, PR^{13} , $PR^{13}R^{14}$, $P(O)R^{15}R^{16}$, and a bond to L_n ;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1 - C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{3-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl- C_{1-10} alkyl substituted with 0-3 R^{17} , C_{1-10} alkyl- C_{6-10} aryl- substituted with 0-3 R^{17} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17} ;

R^{13} and R^{14} are each independently selected from the group: a bond to L_n , hydrogen, C_1 - C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{1-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group

is a 5-10 membered heterocyclic ring system containing
 1-4 heteroatoms independently selected from N, S, and O,
C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀
alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, a 5-10
 5 membered heterocyclic ring system containing 1-4
 heteroatoms independently selected from N, S, and O and
 substituted with 0-3 R¹⁷, and an electron, provided that
 when one of R¹³ or R¹⁴ is an electron, then the other is
 also an electron;

10

alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

15

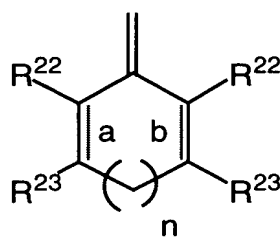
R¹⁵ and R¹⁶ are each independently selected from the group: a
 bond to L_n, -OH, C₁₋₁₀ alkyl substituted with 0-3 R¹⁷,
C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted
 with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷,
heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein
 the heterocyclo group is a 5-10 membered heterocyclic
 ring system containing 1-4 heteroatoms independently
 20 selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl
substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl-
substituted with 0-3 R¹⁷, and a 5-10 membered
 heterocyclic ring system containing 1-4 heteroatoms
 independently selected from N, S, and O and substituted
 25 with 0-3 R¹⁷;

25

30

R¹⁷ is independently selected at each occurrence from the
 group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN,
-CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸,
-OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂,
-NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂,

- NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸,
-S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸,
NO₂, -C(=O)NHR¹⁸, -C(=O)NHN(R¹⁸)R^{18a}, -OCH₂CO₂H,
 5 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆
cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl,
aryl substituted with 0-2 R¹⁸, and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O;
- 10 R¹⁸, R^{18a}, and R¹⁹ are independently selected at each
occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl,
phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and
trifluoromethyl;
- 15 Pg is a thiol protecting group;
- R²⁰ and R²¹ are independently selected from the group: H,
C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂,
C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne
 20 substituted with 0-3 R²³, aryl substituted with 0-3 R²³,
unsaturated 5-10 membered heterocyclic ring system
containing 1-4 heteroatoms independently selected from N,
S, and O and substituted with 0-3 R²³, and unsaturated
C₃-C₁₀ carbocycle substituted with 0-3 R²³;
- 25 alternatively, R²⁰ and R²¹, taken together with the divalent
carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24} ,
C₁-C₁₀ alkyl substituted with 0-3 R^{24} , C₂-C₁₀ alkenyl
 5 substituted with 0-3 R^{24} , C₂-C₁₀ alkynyl substituted with
0-3 R^{24} , aryl substituted with 0-3 R^{24} , a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O and substituted
with 0-3 R^{24} , and C₃-₁₀ carbocycle substituted with 0-3
 10 R^{24} ;

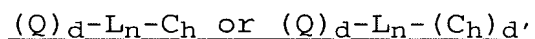
alternatively, R^{22} , R^{23} taken together form a fused aromatic or
a 5-10 membered heterocyclic ring system containing 1-4
heteroatoms independently selected from N, S, and O;

15 **a** and **b** indicate the positions of optional double bonds and **n**
is 0 or 1;

R^{24} is independently selected at each occurrence from the
 20 group: =O, F, Cl, Br, I, -CF₃, -CN, -CO₂ R^{25} , -C(=O) R^{25} ,
-C(=O)N(R^{25})₂, -N(R^{25})₃⁺, -CH₂OR²⁵, -OC(=O) R^{25} ,
-OC(=O)OR^{25a}, -OR²⁵, -OC(=O)N(R^{25})₂, -NR²⁶C(=O) R^{25} ,
-NR²⁶C(=O)OR^{25a}, -NR²⁶C(=O)N(R^{25})₂, -NR²⁶SO₂N(R^{25})₂,
-NR²⁶SO₂ R^{25a} , -SO₃H, -SO₂ R^{25a} , -SR²⁵, -S(=O) R^{25a} ,
 25 -SO₂N(R^{25})₂, -N(R^{25})₂, =NOR²⁵, -C(=O)NHOR²⁵, -OCH₂CO₂H, and
2-(1-morpholino)ethoxy; and,

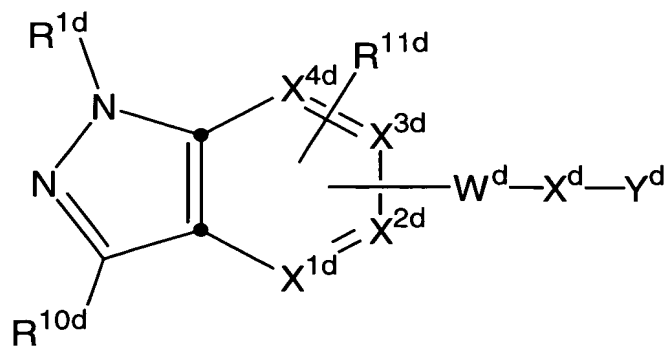
R²⁵, R^{25a}, and R²⁶ are each independently selected at each occurrence from the group: hydrogen and C₁-C₆ alkyl.
~~or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a~~
 5 ~~chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.~~

59. (Amended) A kit according to claim 58 wherein said kit
 10 comprises a plurality of separate containers, wherein at least one of said containers ~~contains a compound of Claim 1, or a pharmaceutically acceptable salt thereof, and at least another~~
~~of said containers contains one or more agents selected from the group consisting of a chemotherapeutic agent and a~~
 15 ~~radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, and~~
another of said containers contains a compound of formula:



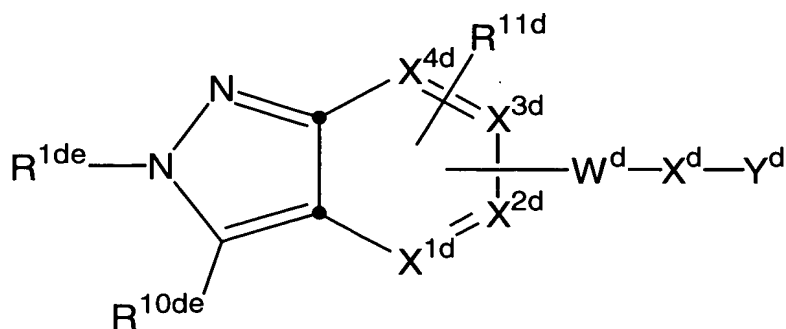
20

wherein, Q is independently a compound of Formula (Ia) or (Ib):



25

(Ia)



(Ib)

including stereoisomeric forms thereof, or mixtures of
 5 stereoisomeric forms thereof, or pharmaceutically
 acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d - X^d - Y^d , or C- L_n ;

X^{2d} is N, CH, or C- W^d - X^d - Y^d ;

10 X^{3d} is N, CR^{11d} , or C- W^d - X^d - Y^d ;

X^{4d} is N or CR^{11d} ;

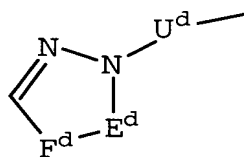
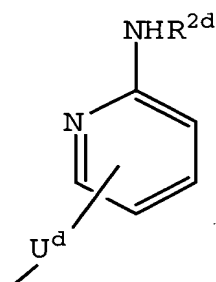
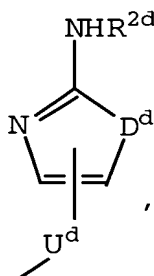
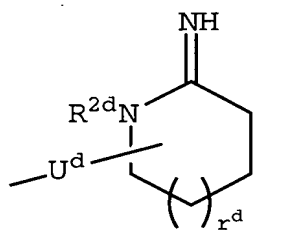
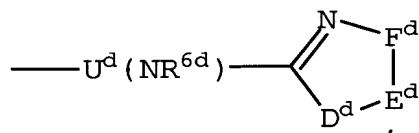
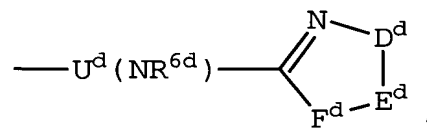
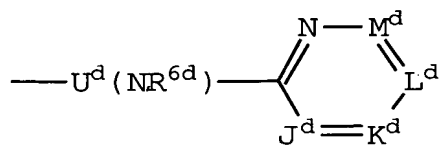
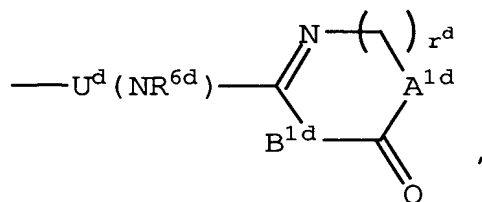
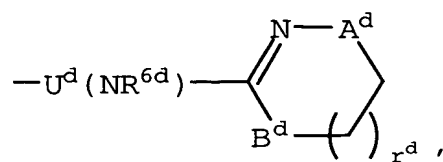
provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d -
 X^d - Y^d , and when R^{10d} is R^{1de} then X^{3d} is C- W^d - X^d - Y^d ;

15

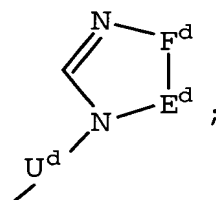
R^{1d} is selected from: R^{1de} , C_1 - C_6 alkyl substituted with 0-1
 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d}
 or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or
 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d}
 or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or
 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d}
 or 0-2 R^{11d} or 0-1 R^{21d} ;

20

R^{1de} is selected from:



or



5

A^d and B^d are independently -CH₂-, -O-, -N(R^{2d})-, or -C(=O)-.

A^{1d} and B^{1d} are independently -CH₂- or -N(R^{3d})-;

D^d is -N(R^{2d})-, -O-, -S-, -C(=O)- or -SO₂-;

5

E^d-F^d is -C(R^{4d})=C(R^{5d})-, -N=C(R^{4d})-, -C(R^{4d})=N-, or
-C(R^{4d})₂C(R^{5d})₂-;

J^d, K^d, L^d and M^d are independently selected from

10 -C(R^{4d})-, -C(R^{5d})- and -N-, provided that at least one of
J^d, K^d, L^d and M^d is not -N-;

R^{2d} is selected from: H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl,
(C₁-C₆ alkoxy)carbonyl; (C₁-C₆ alkyl)aminocarbonyl, C₃-C₆
15 alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl,
heteroaryl(C₁-C₆ alkyl)carbonyl, heteroarylcarbonyl,
aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl-, arylcarbonyl,
C₁-C₆ alkylsulfonyl, arylsulfonyl, aryl(C₁-C₆
alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆
20 alkyl)sulfonyl, aryloxycarbonyl, and aryl(C₁-C₆
alkoxy)carbonyl, wherein said aryl groups are substituted
with 0-2 substituents selected from the group: C₁-C₄
alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro;

25 R^{3d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁
cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and
heteroaryl(C₁-C₆ alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C₁-C₄ alkoxy,

30 NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C₁-C₆ alkyl, C₃-C₆ alkenyl,
C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆

alkyl)-, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl,
and arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d}

5 can be taken together with the carbon atoms to which they
are attached to form a 5-7 membered carbocyclic or 5-7
membered heterocyclic aromatic or non-aromatic ring
system, said carbocyclic or heterocyclic ring being
optionally substituted with 0-2 groups selected from: C₁-
 10 C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, amino, CF₃, and NO₂;

U^d is selected from:

-(CH₂)_n^d-,

-(CH₂)_n^d(CR^{7d}=CR^{8d})(CH₂)_m^d-,

15 -(CH₂)_n^d(C≡C)(CH₂)_m^d-,

-(CH₂)_t^dQ(CH₂)_m^d-,

-(CH₂)_n^dO(CH₂)_m^d-,

-(CH₂)_n^dN(R^{6d})(CH₂)_m^d-,

-(CH₂)_n^dC(=O)(CH₂)_m^d-,

20 -(CH₂)_n^d(C=O)N(R^{6d})(CH₂)_m^d-,

-(CH₂)_n^dN(R^{6d})(C=O)(CH₂)_m^d-, and

-(CH₂)_n^dS(O)_p^d(CH₂)_m^d;

wherein one or more of the methylene groups in U^d is

optionally substituted with R^{7d};

25

Q^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-
phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-
pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

30 R^{6d} is selected from: H, C₁-C₄ alkyl, and benzyl;

R^{7d} and R^{8d} are independently selected from: H, C₁-C₆ alkyl,
C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆
alkyl)-,
and heteroaryl(C₀-C₆ alkyl)-;

5

R^{10d} is selected from: H, R^{1de}, C₁-C₄ alkoxy substituted with
0-1 R^{21d}, N(R^{6d})₂, halogen, NO₂, CN, CF₃, CO₂R^{17d},
C(=O)R^{17d}, CONR^{17d}R^{20d}, -SO₂R^{17d},
-SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1
R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d},
C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d},
C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1
R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1
R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or
0-2 R^{11d} or 0-1 R^{21d};

15

R^{10de} is selected from: H, C₁-C₄ alkoxy substituted with 0-1
R^{21d}, N(R^{6d})₂, halogen, NO₂, CN, CF₃, CO₂R^{17d}, C(=O)R^{17d},
CONR^{17d}R^{20d}, -SO₂R^{17d}, -SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl
substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl
substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl
substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁
cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d},
aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and
aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or
0-1 R^{21d};

20

25

R^{11d} is selected from H, halogen, CF₃, CN, NO₂, hydroxy,
NR^{2d}R^{3d}, C₁-C₄ alkyl substituted with 0-1 R^{21d}, C₁-C₄
alkoxy substituted with 0-1 R^{21d}, aryl substituted with
0-1 R^{21d}, aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{21d},

30

(C₁-C₄ alkoxy)carbonyl substituted with 0-1 R^{21d}, (C₁-C₄ alkyl)carbonyl substituted with 0-1 R^{21d}, C₁-C₄ alkylsulfonyl substituted with 0-1 R^{21d}, and C₁-C₄ alkylaminosulfonyl substituted with 0-1 R^{21d};

5

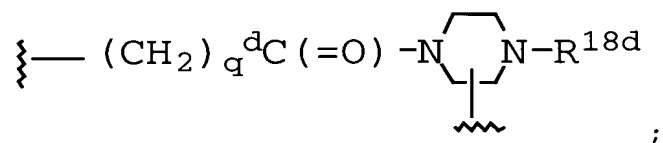
W^d is selected from:

-(C(R^{12d})₂)_q^dC(=O)N(R^{13d})-, and

-C(=O)-N(R^{13d})-(C(R^{12d})₂)_q^d-;

10 X^d is -C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-; or

alternatively, W^d and X^d can be taken together to be



15 R^{12d} is selected from H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, and aryl(C₁-C₆ alkyl)-;

R^{13d} is selected from H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl,
20 and aryl(C₁-C₆ alkyl)-;

R^{14d} is selected from:

H, C₁-C₆ alkylthio(C₁-C₆ alkyl)-, aryl(C₁-C₁₀ alkylthioalkyl)-, aryl(C₁-C₁₀ alkoxyalkyl)-, C₁-C₁₀ alkyl,
25 C₁-C₁₀ alkoxyalkyl, C₁-C₆ hydroxyalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, and CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or

heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d};

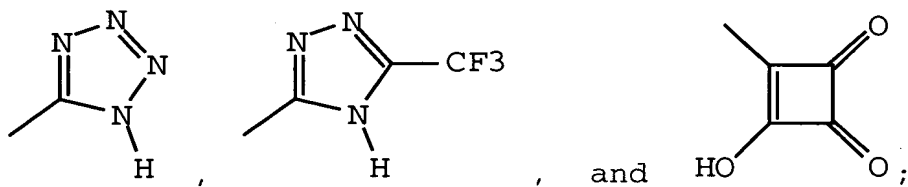
R^{15d} is selected from:

- 5 H, R^{16d}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl,
C₁-C₁₀ alkylaminoalkyl, C₁-C₁₀ dialkylaminoalkyl, (C₁-C₁₀
alkyl)carbonyl, aryl(C₁-C₆ alkyl)carbonyl, C₁-C₁₀ alkenyl,
C₁-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl,
aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl,
10 heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, SO₂R^{17d}, and
SO₂NR^{17d}R^{20d}, provided that any of the above alkyl,
cycloalkyl, aryl or heteroaryl groups may be
unsubstituted or substituted independently with 0-2 R^{11d};

- 15 Y^d is selected from:

-COR^{19d}, -SO₃H, -PO₃H, tetrazolyl, -CONHNHSO₂CF₃, -
CONHSO₂R^{17d}, -CONHSO₂NHR^{17d}, -NHCOCF₃, -NHCONHSO₂R^{17d}, -
NHSO₂R^{17d}, -OPO₃H₂, -OSO₃H, -PO₃H₂, -SO₃H, -SO₂NHCOR^{17d}, -
SO₂NHCO₂R^{17d},

20 _____



R^{16d} is selected from:

- 25 -N(R^{20d})-C(=O)-O-R^{17d},
-N(R^{20d})-C(=O)-R^{17d},
-N(R^{20d})-C(=O)-NH-R^{17d},
-N(R^{20d})SO₂-R^{17d}, and
-N(R^{20d})SO₂-NR^{20d}R^{17d};

R^{17d} is selected from:

C₁-C₁₀ alkyl optionally substituted with a bond to L_n, C₃-C₁₁ cycloalkyl optionally substituted with a bond to L_n, aryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)aryl optionally substituted with a bond to L_n, heteroaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)heteroaryl optionally substituted with a bond to L_n, biaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, heteroaryl optionally substituted with a bond to L_n, aryl optionally substituted with a bond to L_n, biaryl optionally substituted with a bond to L_n, and a bond to L_n, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group consisting of: C₁-C₄ alkyl, C₁-C₄ alkoxy, aryl, heteroaryl, halo, cyano, amino, CF₃, and NO₂;

R^{18d} is selected from:

-H,
-C(=O)-O-R^{17d},
-C(=O)-R^{17d},
-C(=O)-NH-R^{17d},
-SO₂-R^{17d}, and
-SO₂-NR^{20d}R^{17d};

R^{19d} is selected from: hydroxy, C₁-C₁₀ alkyloxy,

C₃-C₁₁ cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀ alkylcarbonyloxyalkyloxy, C₃-C₁₀ alkoxy carbonyloxyalkyloxy, C₂-C₁₀ alkoxy carbonylalkyloxy, C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy, C₅-C₁₀ cycloalkoxy carbonyloxyalkyloxy, C₅-C₁₀ cycloalkoxy carbonylalkyloxy,

C₇-C₁₁ aryloxycarbonylalkyloxy,
C₈-C₁₂ aryloxycarbonyloxyalkyloxy,
C₈-C₁₂ arylcarbonyloxyalkyloxy,
C₅-C₁₀ alkoxyalkylcarbonyloxyalkyloxy, C₅-C₁₀ (5-alkyl-
 5 1,3-dioxo-cyclopenten-2-one-yl)methyloxy, C₁₀-C₁₄ (5-aryl-
1,3-dioxo-cyclopenten-2-one-yl)methyloxy, and
(R^{11d}) (R^{12d})N-(C₁-C₁₀ alkoxy)-;

10 R^{20d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁
cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and
heteroaryl(C₁-C₆ alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}₂;

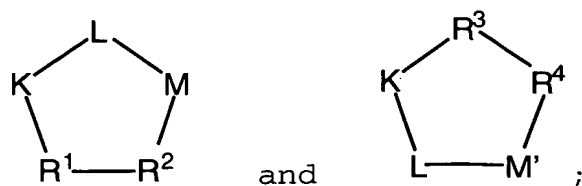
15 m^d is 0-4;
n^d is 0-4;
t^d is 0-4;
p^d is 0-2;
q^d is 0-2; and
r^d is 0-2;

20

with the following provisos:

(1) t^d, n^d, m^d and q^d are chosen such that the number of atoms
connecting R^{1d} and Y^d is in the range of 10-14; and
 (2) n^d and m^d are chosen such that the value of n^d plus m^d is
 25 greater than one unless U^d is
-(CH₂)_t Q^d (CH₂)_m -;

or Q is a peptide selected from the group:



R¹ is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to L_n;

5

R² is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n;

10

R³ is D-valine;

R⁴ is D-tyrosine substituted on the hydroxy group with a bond to L_n;

15

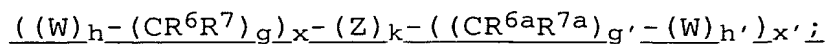
provided that one of R¹ and R² in each Q is substituted with a bond to L_n, and further provided that when R² is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

provided that at least one Q is a compound of Formula (Ia) or (Ib);

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

d' is 1-100;

L_n is a linking group having the formula:



W is independently selected at each occurrence from the group:

O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)N R⁸, C(=O),
C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH,
(OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and
 5 (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰,
 10 C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10
membered heterocyclic ring system containing 1-4
heteroatoms independently selected from N, S, and O and
substituted with 0-3 R¹⁰;

15 R⁶, R^{6a}, R⁷, R^{7a}, and R⁸ are independently selected at each
occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁-C₅
alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3
R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁-C₅ alkoxy
substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹,
 20 NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_H;

R¹⁰ is independently selected at each occurrence from the
group: a bond to C_H, COOR¹¹, C(=O)NHR¹¹, NHC(=O)R¹¹, OH,
NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with
 25 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy
substituted with 0-1 R¹², and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O and substituted
with 0-3 R¹¹;

30 R¹¹ is independently selected at each occurrence from the
group: H, alkyl substituted with 0-1 R¹², aryl

substituted with 0-1 R^{12} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{12} , C_{3-10} cycloalkyl substituted with 0-1 R^{12} , polyalkylene glycol substituted with 0-1 R^{12} , carbohydrate substituted with 0-1 R^{12} , cyclodextrin substituted with 0-1 R^{12} , amino acid substituted with 0-1 R^{12} , polycarboxyalkyl substituted with 0-1 R^{12} , polyazaalkyl substituted with 0-1 R^{12} , and peptide substituted with 0-1 R^{12} , wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to C_h ;

R^{12} is a bond to C_h ;

15

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

20

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

25

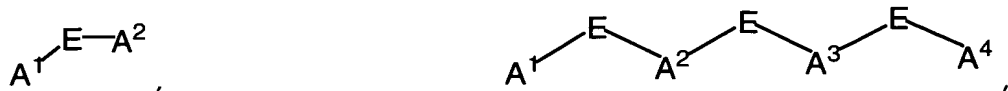
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

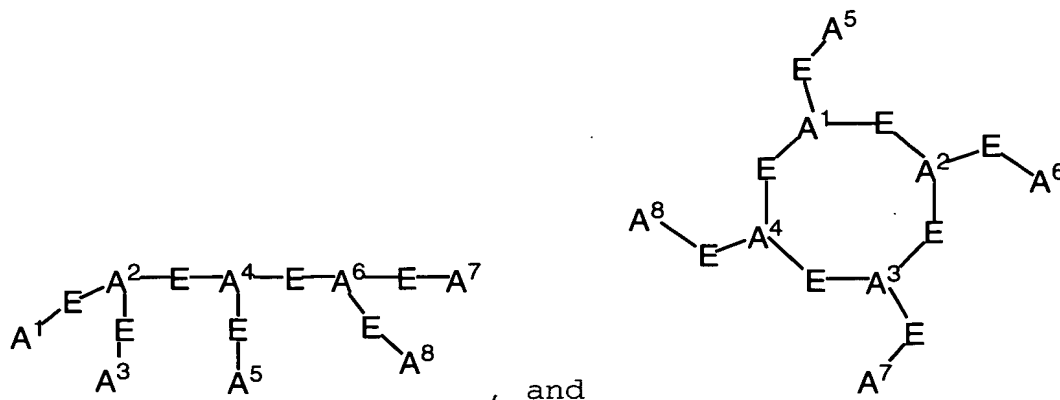
x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

30

C_h is a metal bonding unit having a formula selected from the group:





A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , and A^8 are independently selected at
 5 each occurrence from the group: NR^{13} , $NR^{13}R^{14}$, S, SH, $S(Pg)$, O, OH, PR^{13} , $PR^{13}R^{14}$, $P(O)R^{15}R^{16}$, and a bond to L_n ;

E is a bond, CH, or a spacer group independently selected at
 each occurrence from the group: C_1 - C_{10} alkyl substituted
 10 with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{3-10}
 cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10}
 alkyl substituted with 0-3 R^{17} , wherein the heterocyclo
 group is a 5-10 membered heterocyclic ring system
 containing 1-4 heteroatoms independently selected from N,
 15 S, and O, C_{6-10} aryl- C_{1-10} alkyl substituted with 0-3 R^{17} ,
 C_{1-10} alkyl- C_{6-10} aryl- substituted with 0-3 R^{17} , and a
 5-10 membered heterocyclic ring system containing 1-4
 heteroatoms independently selected from N, S, and O and
 substituted with 0-3 R^{17} ;

20 R^{13} and R^{14} are each independently selected from the group: a
 bond to L_n , hydrogen, C_1 - C_{10} alkyl substituted with 0-3
 R^{17} , aryl substituted with 0-3 R^{17} , C_{1-10} cycloalkyl
 substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl
 25 substituted with 0-3 R^{17} , wherein the heterocyclo group

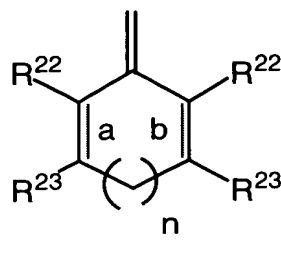
is a 5-10 membered heterocyclic ring system containing
 1-4 heteroatoms independently selected from N, S, and O,
C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀
alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, a 5-10
 5 membered heterocyclic ring system containing 1-4
 heteroatoms independently selected from N, S, and O and
 substituted with 0-3 R¹⁷, and an electron, provided that
 when one of R¹³ or R¹⁴ is an electron, then the other is
 also an electron;

10 alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁵ and R¹⁶ are each independently selected from the group: a
 bond to L_n, -OH, C_{1-C10} alkyl substituted with 0-3 R¹⁷,
 15 C_{1-C10} alkyl substituted with 0-3 R¹⁷, aryl substituted
 with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷,
heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein
 the heterocyclo group is a 5-10 membered heterocyclic
 ring system containing 1-4 heteroatoms independently
 20 selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl
substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl-
substituted with 0-3 R¹⁷, and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O and substituted
 25 with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the
 group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN,
 -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸,
 30 -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂,
 -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂,

- NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸,
-S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸,
NO₂, -C(=O)NHR¹⁸, -C(=O)NHN(R¹⁸)R^{18a}, -OCH₂CO₂H,
 5 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆
cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl,
aryl substituted with 0-2 R¹⁸, and a 5-10 membered
heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O;
- 10 R¹⁸, R^{18a}, and R¹⁹ are independently selected at each
occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl,
phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and
trifluoromethyl;
- 15 Pg is a thiol protecting group;
- R²⁰ and R²¹ are independently selected from the group: H,
C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂,
C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne
 20 substituted with 0-3 R²³, aryl substituted with 0-3 R²³,
unsaturated 5-10 membered heterocyclic ring system
containing 1-4 heteroatoms independently selected from N,
S, and O and substituted with 0-3 R²³, and unsaturated
C₃-C₁₀ carbocycle substituted with 0-3 R²³;
- 25 alternatively, R²⁰ and R²¹, taken together with the divalent
carbon radical to which they are attached form:



R^{22} and R^{23} are independently selected from the group: H, R^{24} , C_1 - C_{10} alkyl substituted with 0-3 R^{24} , C_2 - C_{10} alkenyl substituted with 0-3 R^{24} , C_2 - C_{10} alkynyl substituted with 0-3 R^{24} , aryl substituted with 0-3 R^{24} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{24} , and C_{3-10} carbocycle substituted with 0-3 R^{24} ;

alternatively, R^{22} , R^{23} taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R^{24} is independently selected at each occurrence from the group: =O, F, Cl, Br, I, $-CF_3$, $-CN$, $-CO_2R^{25}$, $-C(=O)R^{25}$, $-C(=O)N(R^{25})_2$, $-N(R^{25})_3^+$, $-CH_2OR^{25}$, $-OC(=O)R^{25}$, $-OC(=O)OR^{25a}$, $-OR^{25}$, $-OC(=O)N(R^{25})_2$, $-NR^{26}C(=O)R^{25}$, $-NR^{26}C(=O)OR^{25a}$, $-NR^{26}C(=O)N(R^{25})_2$, $-NR^{26}SO_2N(R^{25})_2$, $-NR^{26}SO_2R^{25a}$, $-SO_3H$, $-SO_2R^{25a}$, $-SR^{25}$, $-S(=O)R^{25a}$, $-SO_2N(R^{25})_2$, $-N(R^{25})_2$, $=NOR^{25}$, $-C(=O)NHOR^{25}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and,

R²⁵, R^{25a}, and R²⁶ are each independently selected at each occurrence from the group: hydrogen and C₁-C₆ alkyl.

65. (Amended) A therapeutic ~~metallopharmaceutical~~
radiopharmaceutical composition comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a radiopharmaceutical comprising:

a) a therapeutic metal; and

b) a compound;

wherein the compound comprises:

i) a chelator capable of chelating the therapeutic metal;

ii) a targeting moiety; and

iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof,

wherein the targeting moiety is an indazole nonpeptide that binds to a receptor that is upregulated during angiogenesis.

~~according to claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, further comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.~~

66. (Amended) A therapeutic radiometallopharmaceutical composition according to claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin,

nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

10

67. (Amended) A therapeutic radiometal pharmaceutical composition according to claim 65, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

20

68. (Amended) A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof wherein the therapeutic radiopharmaceutical comprises:

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a) a therapeutic metal; and

b) a compound;

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wherein the compound comprises:

- i) a chelator capable of chelating the therapeutic metal;
- ii) a targeting moiety; and
- iii) 0-1 linking groups between the targeting moiety and chelator; or

a pharmaceutically acceptable salt thereof;
wherein the targeting moiety is an indazole non-peptide that
binds to a receptor that is upregulated during angiogenesis. of
~~Claim 19 or a pharmaceutically acceptable salt thereof, and at~~
5 ~~least one agent selected from the group consisting of a~~
~~chemotherapeutic agent and a radiosensitizer agent, or a~~
~~pharmaceutically acceptable salt thereof.~~